

## **REMARKS AND RESPONSES**

Claims 1-4 and 21-25 are pending in the present application. Claims 1-3, and 21-24 are withdrawn as directed to a non-elected invention. Claims 4 and 25 are currently under consideration. By this response, Applicant amends claims 1 and 4. Support for the amendments is found in the specification and claims as originally filed. Accordingly, the amendments do not add any new matter. Reconsideration of the pending claims in view of the foregoing amendments and following remarks is respectfully requested. Applicant respectfully requests the amendments be entered because they place the case in condition for allowance or reduce the issues on appeal. Applicant further submits that the proposed amendments do not raise any additional new issues or require any further searching by the Examiner.

### **1. Election/Restriction**

Applicant acknowledges that the restriction requirement and election of Group I was made final in Paper No. 18 mailed on December 12, 2003. Nonetheless, Applicant has amended claim 1 to be generally directed to determining expression of *Wnt5a* wherein increased expression of *Wnt5a* in the test sample compared to *Wnt5a* expression in a tumor having less than about 3.5% invasive ability indicates the tumor is aggressive. Basis for this amendment is found in the specification as originally filed, for example in Table 1. In view of this amendment Applicant respectfully requests that claims 1-3 be rejoined to Group I.

Applicant respectfully submits that the prior art of record fails to teach or suggest a method of diagnosing an aggressive form of cancer by providing a genetic sample from a test sample of a tumor; determining expression of

*Wnt5a* wherein increased expression of *Wnt5a* in the test sample compared to *Wnt5a* expression in a tumor having less than about 3.5% invasive ability indicates the tumor is aggressive. Therefore, Applicant submits claim 1 is allowable over the art of record.

Because claims 2-3 incorporate the limitations of claim 1, claims 2-3 are allowable for at least the reasons claim 1 is allowable.

## **2. Drawings**

The Office Action notes that a Petition to Accept Colored Drawings was not received by the USPTO with the Response mailed by Applicant on April 12, 2004. Applicant encloses a copy of the Petition submitted on April 12, 2004, having a signed Certificate of Mailing indicating that the Petition was indeed filed on April 12, 2004. Additionally, Applicant encloses a copy of the return postcard listing the Petition and having a USPTO date-stamp of April 14, 2004, indicating the Petition was received by the USPTO. Accordingly, Applicant requests that the Petition be entered into the record.

## **3. Rejections under 35 U.S.C. § 112**

Claims 4 and 25 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Office Action indicates that it is allegedly unclear how the expression pattern of the genes is related to the determination of aggressive or non-aggressive tumors.

Applicant amended claim 4 to recite "wherein increased expression of *Wnt5a* in the test sample compared to *Wnt5a* expression in a tumor having non-detectable or no vasculogenic mimicry indicates the tumor is aggressive".

By this amendment, Applicant has provided the nexus between *Wnt5a* expression and aggressive tumors. Basis for this amendment is found in the specification as originally filed, for example, in Table 1. In view of this amendment, the rejection of claim 4 is moot. Because claim 25 depends from claim 4, the rejection is also moot for claim 25.

#### **4. Rejections under 35 U.S.C. § 103**

Claims 4 and 25 are rejected under 35 U.S.C. § 103 as allegedly obvious over *Iozzo et al.* (1995) Cancer Research, 55:3495-3499. Applicant respectfully traverses this rejection.

##### **4.1. Relevant Law**

The United States Patent and Trademark Office (USPTO) has the burden of showing a prima facie case of obviousness. *In re Bell*, 991 F.2d 781, 783 (Fed. Cir. 1993). In determining obviousness, the invention must be considered as a whole, and the claims must be considered in their entirety. *Medtronic, Inc. v. Cardiac Pacemakers, Inc.*, 721 F.2d 1563, 1567 (Fed. Cir. 1983). A prima facie case of obviousness is established when the teachings from the prior art itself would have suggested the claimed subject matter to a person of ordinary skill in the art. *In re Rhinehart*, 531 F.2d 1048, 1051 (CCPA 1976). More specifically, the requirements for establishing a prima facie case of obviousness include: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations.

When a rejection depends on a combination of prior art references, the USPTO must show that there is some teaching, suggestion, or motivation to combine the references. *In re Geiger*, 815 F.2d 686, 688 (Fed. Cir. 1987). The mere fact that the prior art could be modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984). The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Finally, obviousness may not be established using hindsight. *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1551 (Fed. Cir. 1983).

#### **4.2 Analysis**

The Office Action alleges that it would have been obvious to one of ordinary skill in the art to modify the teachings of *Iozzo et al.* to include a step of selecting a treatment regimen to treat an individual diagnosed with the aggressive or non-aggressive tumors because it is conventional in the field of oncology for clinicians to present the patient with some type of treatment option to lower the risk of mortality.

The Office Action further notes that Applicant's previous arguments were found unpersuasive because Applicant allegedly argued limitations that were not in the claims. Applicant has amended claim 4 as noted above to recite "wherein increased expression of *Wnt5a* in the test sample compared to *Wnt5a* expression in a tumor having non-detectable or no vasculogenic mimicry indicates the tumor is aggressive". Applicant further amended the claim to clarify that a different treatment regimen is selected if the tumor is aggressive versus non-aggressive. Basis

for the amendments are found in the specification as originally filed, for example, in Table 1.

Applicant respectfully submits that *Iozzo et al.* fails to teach or suggest a method of diagnosing an aggressive form of malignant melanoma by providing a genetic sample from a test sample of a tumor; determining expression of *Wnt5a* wherein increased expression of *Wnt5a* in the test sample compared to *Wnt5a* expression in a tumor having non-detectable or no vasculogenic mimicry indicates the tumor is aggressive; and selecting a first treatment regimen for an individual with the tumor if the tumor is aggressive and a second treatment regimen if the tumor is non-aggressive, wherein the first and second treatment regimens are not the same.

Moreover, Applicant submits that there is no teaching or suggestion in the prior art of record to modify *Iozzo et al.* to arrive at the claimed subject matter. Accordingly, the claims as amended are not obvious, and the rejection should be withdrawn.

**Conclusion**

For at least the foregoing reasons, Applicant submits that all rejections and objections have been addressed or rendered moot and that claims 1-4 and 25 are in condition for allowance.

If the Examiner believes that a telephone conference would expedite the examination of the above-identified patent application, the Examiner is invited to call the undersigned.

No fee is believed to be due in connection with this amendment and response. If, however, any fee is believed to be due, the Commissioner is hereby authorized to charge any such fee to deposit account No. 50-1078.

Respectfully submitted,



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